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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	PAPER NUMBER
1645	18

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/921,157	Applicant(s) Covacci et al.
	Examiner S. Devi, Ph.D.	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 17, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *38 and 41-46* is/are pending in the application.

4a) Of the above, claim(s) *41-43* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *38 and 44-46* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 03/17/03 (paper no. 16) in response to the non-final Office Action mailed 10/15/02 (paper no. 12). With this, Applicants have amended the specification.

Status of Claims

2) Claims 39 and 40 have been canceled via the amendment filed 03/17/03.

Claims 38 and 44 have been amended via the amendment filed 03/17/03.

New claims 45 and 46 have been added via the amendment filed 03/17/03.

Claims 38 and 41-46 are pending.

Claims 38, 44, 45 and 46 are under examination.

Information Disclosure Statement

3) Acknowledgment is made of Applicants' information disclosure statement filed 02/03/03 (paper no. 14). The information referred to therein has been considered and a signed copy of the same is attached to this Office Action (paper no. 18).

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

The Del Giudice Declaration

6) Acknowledgment is made of Applicants' submission of the Del Giudice Declaration filed 03/17/03 (paper no. 17) under 37 C.F.R. § 1.132, which has been fully considered.

Objection(s) Moot

7) The objection to claim 39 made in paragraph 14 of the Office Action mailed 10/15/02 (paper no. 12) is moot in light of Applicants' cancellation of the claim.

Objection(s) Withdrawn

8) The objection to the drawings made in paragraph 7 of the Office Action mailed 10/15/02 (paper no. 12) is withdrawn in light of the Draftsperson's acceptance of the formal drawings submitted 03/17/03 (paper no. 15).

9) The objection to the specification made in paragraph 8(a) of the Office Action mailed 10/15/02 (paper no. 12) is withdrawn in light of Applicants' amendment to the specification.

10) The objection to the specification made in paragraph 8(b) of the Office Action mailed 10/15/02 (paper no. 12) is withdrawn in light of Applicants' amendment to the specification.

11) The objection to the specification made in paragraph 8(d) of the Office Action mailed 010/15/02 (paper no. 12) is withdrawn in light of Applicants' amendment argument.

Rejection(s) Moot

12) The rejection of claim 39 made in paragraphs 10(c), 10(e) and 10(f) of the Office Action mailed 10/15/02 (paper no. 12) under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

13) The rejection of claim 40 made in paragraph 10(g) of the Office Action mailed 10/15/02 (paper no. 12) under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

14) The rejection of claims 39 and 40 made in paragraph 11 of the Office Action mailed 10/15/02 (paper no. 12) under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not adequately described, is moot in light of Applicants' cancellation of the claims.

15) The rejection of claims 39 and 40 made in paragraph 12 of the Office Action mailed 10/15/02 (paper no. 12) under 35 U.S.C. § 112, first paragraph, as being non-enabled, is moot in light of Applicants' cancellation of the claims.

Rejection(s) Withdrawn

16) The rejection of claim 38 made in paragraph 10(a) of the Office Action mailed 10/15/02 (paper no. 12) under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

17) The rejection of claims 38 and 44 made in paragraph 10(b) of the Office Action mailed 10/15/02 (paper no. 12) under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

18) The rejection of claims 38 and 44 made in paragraph 10(e) of the Office Action mailed 10/15/02 (paper no. 12) under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

Rejection(s) Maintained

19) The provisional rejection of claims 38 and 44 made in paragraph 9 of the Office Action mailed 10/15/02 (paper no. 12) under the judicially created doctrine of obviousness-type double patenting over the cited claims of the co-pending application, 09/360,934, is maintained for reasons set forth therein. It is noted that Applicants have agreed to submit a terminal disclaimer over SN 09/360,934 upon indication of allowability of the claims.

20) The rejection of claims 38 and 44 made in paragraph 10(d) of the Office Action mailed 10/15/02 (paper no. 12) under 35 U.S.C. § 112, second paragraph, as being indefinite, is maintained for reasons set forth therein and herebelow.

New claims 45 and 46 are now added to this rejection.

Applicants cite case law and contend that the term 'substantially' is a term routinely used in the field of biotechnology. Applicants state that the term is used in the claims to 'avoid a strict numerical boundary to the specified parameter'. Applicants submit a copy of the Del Giudice Declaration previously submitted in application SN 09/360,934 and state that the Declaration asserts the term 'substantially' to be understood by those of ordinary skill in the art to mean that *Helicobacter pylori* proteins, or fragments thereof, do not exhibit 'statistically significant cytotoxic effects' and thus would be acceptable for use in human vaccines. Applicants cite several issued patents the claims of which apparently include the limitation "substantially pure and isolated" or "substantially free of" etc.

Applicants' arguments have been carefully considered, but are non-persuasive. The limitations such as, "substantially no toxicity"; "substantially reduced toxicity" and "substantially reduced contribution to toxicity", because it is unclear what degree of toxicity qualifies as substantially no toxicity or substantially reduced toxicity. The specification does not appear to provide a standard for ascertaining the requisite degree of toxicity that qualifies as "substantially no toxicity" and "substantially reduced toxicity". The term "substantially" is a relative term which renders the metes and bounds of the claims indeterminate. The definition or meaning of "substantially

no toxicity"; "substantially reduced toxicity" and "substantially reduced contribution to toxicity" is not equated 'statistically significant cytotoxic effects' in the specification as originally filed. How to obtain cytotoxin fragments of 'statistically significant cytotoxic effects' is described in the specification. It is important to note that unlike the claims of other issued patents identified by Applicants, the polypeptide in the currently claimed composition is neither identified as 'isolated' nor 'purified'. The toxicity is not specified and therefore encompasses cytotoxicity, endotoxicity, exotoxicity, cell-vacuolizing toxicity, or any other type of general toxicity. What exact toxicity and what degree of toxicity are encompassed in the limitation: 'substantially no toxicity' or 'substantially reduced toxicity', is not understood. The terms 'substantially no toxicity' and 'substantially reduced toxicity' are not specifically defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and therefore, one of ordinary skill in the art would not be reasonably appraised of the scope of the claims. With regard to Applicants' mentioning of the prosecution of unrelated patents and the claim language used in the instant invention, it should be noted that the prosecution history of previous patent applications is irrelevant to the prosecution of the instant application. The prosecution of one application does not have to duplicate that of a previous application. Each case is individually evaluated and prosecuted on its own merits based on the definition provided in that particular application.

21) The rejection of claims 38 and 44 made in paragraph 12 of the Office Action mailed 10/15/02 (paper no. 12) under 35 U.S.C. § 112, first paragraph, as being non-enabled, is maintained for reasons set forth therein and herebelow.

New claims 45 and 46 are now added to this rejection.

Applicants point to page 5, lines 35-39 of the specification and state that the term 'toxicity' refers to 'cytotoxicity'. Applicants argue that the specification at page 5, lines 31-39 teaches that the processed 100 kDa polypeptide possesses cytotoxic activity. Applicants submit that 'cytotoxin' is defined in the specification to include the precursor protein having a molecular weight of 140 kDa and fragments and derivatives thereof. Applicants assert that the specification discloses a representative example in which the cytotoxicity of the cytotoxin is determined by measuring the vacuolizing activity of the polypeptide on HeLa cells as well as methods of preparing and testing antisera against the cytotoxin. The Del Giudice Declaration, submitted in response to a rejection in a

different application, provides the reference of Manetti *et al.* (*Infect. Immun.* 63: 4476-4480, 1995) and states that chemically inactivated and genetically detoxified toxins were known to those of skill in the art prior to 02 March 1992. Manetti *et al.* is stated as citing Pizza's (1989) studies about chemically and genetically detoxified subunits of pertussis toxin, which were capable of inducing protective immunity. The Declaration submits that methods of producing protein fragments by recombinant expression techniques and testing the fragments for cytotoxicity by *in vitro* vacuolation assays, and for immunogenicity by immunization, were known in the art. Applicants assert that 'using the application as a guide' one of ordinary skill in the art would have been able to determine which cytotoxin polypeptides are immunologically identifiable by an antibody that reacts specifically with *Helicobacter pylori* cytotoxin and exhibits substantially no cytotoxicity or substantially reduced cytotoxicity.

Applicants' arguments have been carefully considered, but are non-persuasive. It is noted that what is claimed in the instant claims is a 'cytotoxin' which "exhibits substantially no toxicity", "substantially reduced toxicity", or "substantially reduced contribution to toxicity". The only place where these phrases were mentioned in the specification as originally filed was in some original claims. The amendment filed 08/02/01 introduced these phrases in the paragraph bridging pages 3 and 4 of the specification. Other than this brief mentioning, there is no direction and guidance as to how to produce either a full length cytotoxin of SEQ ID NO: 3 or fragments thereof, including recombinant ones, which possess the two required functions: i) substantially no cytotoxicity, substantially reduced cytotoxicity, or substantially reduced contribution to cytotoxicity; and ii) immunological identifiability by an antibody that reacts specifically with *Helicobacter pylori* cytotoxin. A 100 kDa 'fragment' for example of the precursor protein is 'cytotoxic' as opposed to 'substantially non-cytotoxic' (see page 5, last paragraph). The definition for 'cytotoxin' provided in the instant specification is a non-limiting definition which does not exclude a processed 100 kDa polypeptide possessing cytotoxic activity. The genetic detoxification alluded to in the Del Giudice Declaration was not contemplated in the instant specification, as originally filed. Nowhere in the specification can one find the direction and guidance to produce detoxified cytotoxins of *Helicobacter pylori*, or their fragments, such that they possess substantial non-cytotoxicity, or substantially reduced cytotoxicity, or show substantially reduced contribution to cytotoxicity and at

the same time remain immunologically identifiable by an antibody that reacts specifically with *Helicobacter pylori* cytotoxin. The teaching in the specification is contrary to this. For example, at page 7, lines 33-37, the specification teaches polypeptide molecules having amino acid substitutions 'that do not substantially affect the functional aspects', i.e., cytotoxin polypeptides having amino acid substitutions such that their cytotoxic activity remains substantially the same as the native polypeptide. Therefore, using the application as a guide, one of ordinary skill in the art would have been able to produce cytotoxin polypeptides that retain substantial cytotoxicity. The specification, for example, in the second paragraph on page 7 mentions about conservative amino acid replacement and states that 'it is reasonably predictable that an isolated replacement of a leucine with isoleucine ... or a similar conservative replacement of an amino acid with a structurally related amino acid will not have a major effect on the biological activity'. The biological activity includes cytotoxicity. Therefore, it is reasonable to conclude that the retention of immunologic identifiability concurrently with the substantial attenuation of cytotoxocity of a cytotoxin is not predictable without a clear showing, and would have required considerable amount of undue experimentation. Furthermore, with regard to the process of detoxification, the Del Giudice Declaration cites the reference of Mannetti *et al.* (*Infect. Immun.* 63: 4476-4480, 1995). This post-filing publication provides the *prima facie* evidence that in 1995, about three years after the effective filing date of the instant invention, there was no predictability in obtaining the claimed detoxified *Helicobacter pylori* cytotoxin polypeptide variants/fragments that are conformationally competent and therefore immunolgically functional. Mannetti *et al.* taught the conformational complexity of the *Helicobacter pylori* cytotoxin polypeptide. Manetti *et al.* also taught that the immune response is primarily due to conformational epitopes. Manetti *et al.* specifically taught that "[e]ven partial destruction of the conformational epitopes by chemical inactivation can result in lowering of the effective immunogenicity". With regard to the genetic detoxification, Manetti *et al.* in 1995 stated that a "genetically detoxified molecule which retains the native structure **will be** an important goal" (see page 4479), thus indicating that genetic detoxification of *Helicobacter pylori* cytotoxin was not achieved at least until 1995. Pizza's disclosure on pertussis toxin cannot and does not provide enablement for the structurally unrelated *Helicobacter pylori* cytotoxin polypeptide. Although one may be able to produce fragments of SEQ ID NO: 3 and test their cytotoxicity and immunological

identifiability, given the art-disclosed conformational complexity and functional unpreditcability, the maintenance of immunological identifiability by an antibody specifically reactive with the native cytotoxin polypeptide along with the concurrent acquisition of the desired attenuation in cytotoxic activity following one or more amino acid substitutions in the cytotoxin polypeptide, would not have been predictable, absent a concrete showing. Regardless of the complexity or simplicity of the method of isolation and method of testing, conception cannot be achieved until reduction to practice has occurred. Adequate enablement requires more than a mere statement that its is a part of the invention and a reference to a potential method of isolating or testing it. In light of the unpredictability disclosed in the art and the Manetti's teachings, it does not appear that Applicants were in possession of the claimed product, wherein the product is required to possess the two specific functions recited in the claims. The courts have held that it is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. See *Genentech Inc., v. Novo Nordisk A/S Ltd., 42 USPQd 1001.* Moreover, the specification must have been enabling at the time the invention was made and developments after the time of filing are of no consequence to what one skilled in the art would have believed at the time of filing (*In re Wright, 27 USPQ2d 1510, Federal Ceircuit, 1993*). Given the relatively incomplete understanding in the biotechnological field involved, and the lack of a reasonable correlation between the absence of disclosure in the specification as to how to obtain a cytotoxin of substantially reduced or no toxicity which maintains its immunological functions, and the broad scope of protection sought in the claims, the claims are viewed as being non-enabled with regard to the full scope.

Rejection(s) under 35 U.S.C. § 112, First Paragraph

22) Claims 38 and 44- 46 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Instant claims include the new limitation: " .....immunologically identifiable by an antibody which reacts specifically with *Helicobacter pylori* cytotoxin" and exhibits substantially no toxicity, or substantially reduced toxicity, or substantially reduced contribution to toxicity. Applicants state that

this limitation is supported in the specification at page 45, line 26 to page 46, line 6. However, this part of the specification pointed to by Applicants does not provide support for a cytotoxin polypeptide of the amino acid sequence of SEQ ID NO: 3, recombinantly produced or otherwise, and a fragment thereof that is immunologically identifiable by an antibody which reacts specifically with *Helicobacter pylori* cytotoxin **and** which at the same time is immunologically identifiable by an antibody that reacts specifically with *H. pylori* cytotoxin, as recited. Therefore, the limitation in the claims is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to remove the new matter from the claim(s), or invited to point to specific pages and line numbers in the specification where support for such a recitation can be found.

Rejection(s) under 35 U.S.C. § 102

23) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> **(e)** The invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

24) Claims 44 and 46 are rejected under 35 U.S.C. § 102(e) as being anticipated by Cover *et al.* (US 6,054,132, filed 02/26/1992).

The limitation "toxicity" in this rejection is interpreted as encompassing toxicity due to endotoxin. It is also noted that the limitation "toxicity" encompasses general toxicity. It is further noted that the transitional recitation "comprising" is open-ended claim language and therefore does not exclude additional, unrecited elements. See MPEP 2111.03 [R-1].

Cover *et al.* ('132) disclosed antigenic fragments of a cell vacuolating toxin (i.e., cytotoxin) of *Helicobacter pylori* which is recombinantly or synthetically produced and a composition

comprising the same (see column 2, lines 25-58). A 23 amino acid-long N terminal fragment of the toxin antigen, i.e., SEQ ID NO: 1, obtained from the purified toxin is taught (see column 10, lines 2--4; and first sequence in columns 17 and 18 under Sequence Listing). This 23 amino acid-long antigenic fragment of the prior art has 100% sequence identity with a 23 amino acid-long contiguous fragment that stretches between positions 34-56 of the instantly recited SEQ ID NO: 3. The antigenic fragment is present along with water, phosphate buffered saline or an adjuvant (see column 18, third paragraph; column 17, second paragraph; and column 16, lines 45-50). That the 23 amino acid-long fragment of the prior art obtained from a purified toxin is pure enough to be of substantially no endotoxicity or exhibits substantially reduced contribution to LPS-related toxicity, and that it is long enough to be immunologically identifiable by an *H. pylori*-specific antibody are inherent from the teachings of Cover *et al.* Given that all the structural elements of the instant claims are met by the prior art antigenic fragment, the immunological identifiability by an antibody specifically reactive with *H. pylori* cytotoxin and the exhibition of substantially no toxicity or of substantially reduced contribution to toxicity, are viewed as the inherent properties inseparable from the antigenic fragment taught by Cover *et al.* ('132).

Claims 44 and 46 are anticipated by Cover *et al.* ('132).

25) Claims 44 and 46 are rejected under 35 U.S.C. § 102(e) as being anticipated by Cover *et al.* (*J. Biol. Chem.* 267: 10570-10575, 25 May 1992 - Applicants' IDS) (Cover *et al.*, 1992).

The limitation "toxicity" in this rejection is interpreted as encompassing toxicity due to endotoxin. It is also noted that the limitation "toxicity" encompasses general toxicity. It is further noted that the transitional recitation "comprising" is open-ended claim language and therefore does not exclude additional, unrecited elements. See MPEP 2111.03 [R-1].

Cover *et al.* (1992) disclosed an antigenic N-terminal fragment of a cell vacuolating toxin (i.e., cytotoxin) of *Helicobacter pylori* which is recombinantly or synthetically produced and a composition comprising the same in distilled water (see Table III and page 10571, left column). This 23 amino acid-long fragment obtained from the purified toxin antigen has 100% sequence identity with a 23 amino acid-long contiguous fragment that stretches between positions 34-56 of the instantly recited SEQ ID NO: 3. That the 23 amino acid-long fragment of the prior art obtained from a purified toxin is pure enough to be of substantially no endotoxicity or exhibits substantially

reduced contribution to LPS-related toxicity, and that it is long enough to be immunologically identifiable by an *H. pylori*-specific antibody are inherent from the teachings of Cover *et al.* Given that all the structural elements of the instant claims are met by the prior art antigenic fragment, the immunological identifiability by an antibody specifically reactive with *H. pylori* cytotoxin and the exhibition of substantially no toxicity or of substantially reduced contribution to toxicity, are viewed as the inherent or intrinsic properties inseparable from the antigenic fragment taught by Cover *et al.* (1992).

Furthermore, the term "recombinantly produced" in the claim represents a process limitation. When claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown the underlying structure of the prior art antigenic polypeptide fragment differs from that of the instantly claimed fragment of the amino acid sequence of SEQ ID NO: 3.

Claims 44 and 46 are anticipated by Cover *et al.* (1992).

Relevant Prior Art

26) The prior art made of record and not currently relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

- Cover *et al.* (US 5,721,349 and US 6,013,463) disclosed antigenic fragments of a toxic polypeptide of *Helicobacter pylori* that show sequence similarity to the instantly claimed SEQ ID NO: 3 (see entire document).

Remarks

27) Claims 38 and 44-46 stand rejected.

28) Applicants' amendment necessitated the new ground(s) of rejection presented in this Office

action. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

29) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which is able to receive transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

30) Any inquiry concerning this communication or earlier communication(s) from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A message may be left on the Examiner's voice mail service. The Examiner can normally be reached on Monday to Friday from 7.15 a.m to 4.15 p.m. except one day each bi-week which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

S. DEVI, PH.D.
PRIMARY EXAMINER

May, 2003